UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,503	03/04/2005	Akira Suzuki	05273.0096-00000	9248

22852 7590 08/20/2008

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER	
HAIDER, SAIRA BANO	

ART UNIT	PAPER NUMBER
1796	

MAIL DATE	DELIVERY MODE
08/20/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,503	SUZUKI ET AL.	
	Examiner	Art Unit	
	SAIRA HAIDER	1796	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7,11-16 and 19-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7,11-16 and 19-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/27/2008 has been entered.

Claim Rejections - 35 USC § 103

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 1-4, 7, 11-16, and19-22 are rejected under 35 U.S.C. 103(a) as being obvious over Suzuki et al. (WO/01/83594) in view of Lenk et al. (US 5,948,441).

4. The citations for the Suzuki reference are derived from the English Language Equivalent: US 2003/0094715 A1.

5. Suzuki discloses a method for the preparation of microspheres from an emulsion, comprising the following circulation steps: formation of an emulsion, filling the emulsion in a vessel (microsphere storage tank), filtering the emulsion, evaporating the organic phase, and collecting microspheres [0122-0126; 0153].

6. The emulsion has an organic phase containing an organic solvent having a boiling point lower than that of water, a hardly-water-soluble biodegradable polymer, and a medicament, the organic phase is emulsified in an aqueous phase [0039, 0046]. The emulsification takes place in an emulsifying apparatus via a homogenizer [0052, 0159].

7. A portion of the aqueous phase of the emulsion is carried out by passing the emulsion though a filter (e.g. a stainless mesh filter, a glass filter, a ceramic filter) [0118]. The filtered emulsion is circulated to a hollow fiber membrane which evaporates the organic solvent [0113-0118].

8. Suzuki discloses dissolving or dispersing the medicament in a solution of the polymer and the organic solvent [0039-0043]. Suitable organic solvents include halogenated aliphatic hydrocarbon solvents [0044]. In the emulsifying step, the homogenizer operates at a speed of 2,500 rpm and is thus considered high-speed [0159]. It is noted that transfer of the emulsion from the emulsifying apparatus to the vessel is disclosed as being a batch process step [0139], wherein Suzuki exemplifies a vessel which is about 226 times larger than the emulsifying vessel [0159-0161]. The aqueous phase is present in an amount of 1 to 10,000 parts by volume per 1 part by volume of the organic phase [0055]. Suitable polymers include the polyester of a hydroxyfatty acid [0047]. The microspheres are collected via centrifugation [0142]. The microspheres can be dispersed in an excipient and solidified by lyophilization [0148].

9. Suzuki fails to disclose the (1) utilization of a cross-flow filter wherein the filtrate is recycled into the emulsifying apparatus, and (2) evaporation of the organic solvent inside the vessel.

10. In reference to the first deficiency of Suzuki, attention is directed towards the Lenk et al. reference. Lenk discloses a method for the size separation of particles via tangential flow filtration (or cross flow filtration). Lenk discloses that cross flow filtration is better than traditional filtration process (such as ceramic filtration) because it prevents filter cake build-up in the filter surface, eliminates dead-end extrusion of larger particles, and allows for the maintenance of the flow rate of the liquid as it is passed over the membrane (abstract; col. 1, lines24-46). Lenk discloses that cross flow filtration is useful in the separation and classification of emulsions according to size (col. 7, lines 31-34). Additionally, Lenk recognizes that cross flow filtration can be done aseptically, and that

the process can be used to remove unentrapped bioactive agent (col. 7, lines 35-38; col. 8, lines 14-15). It would have been obvious to one of ordinary skill in the art at the time of the invention to utilize the cross flow filter of Lenk in place of the ceramic filter in the invention of Suzuki in order to size the emulsion (and thus size the resulting microspheres), in order to prevent filter cake build-up, eliminate dead-end extrusion of larger particles, and remove the unentrapped bioactive agent (medicament). Specifically, it is noted that it would have been obvious to recycle the unentrapped bioactive agent and utilize it in the formation of the emulsion. The motivation to recycle the unentrapped bioactive agent in the aqueous phase is to prevent adherence of the medicament to the outside of the formed microspheres. Wherein it is undesirable to have the medicament adhered to the outside of the microspheres as recognized by Suzuki [0144].

11. Suzuki in combination with Lenk fails to disclose evaporation of the organic solvent inside the vessel, it is noted that Suzuki discloses this limitation, but it is not in combination with the filtration. However, it would have been obvious to one of ordinary skill in the art at the time of the invention to evaporate the organic solvent inside the vessel in the process taught by the combination of Suzuki and Lenk. The motivation is to minimize the risk of clogging of the hollow fibers since the emulsion is not passing though the hollow fibers, as in the circulation method, rather the emulsion is contacting the outside of the follow fibers [0014, 0121, 0129]. Thus, instead of circulating the emulsion through the hollow fibers in order to remove the organic solvent, the immersion method is utilized.

12. In reference to claim 3, Suzuki discloses transfer of the emulsion into the vessel as a batch step, wherein, it has been held that continuous operation is obvious in view of the batch process of the prior art. *In re Dilnot*, 319 F.2d 188, 138 USPQ 248 (CCPA 1963). Thus, it would have been

obvious to continuously transfer the emulsion into the vessel in the process taught by the combination of Suzuki and Lenk.

13. In reference to claims 11 and 13, the Lenk reference discloses that as the filtrate is collected from the cross flow filter it is desirable to add in a solution at the same rate as which the filtrate is removed in order to maintain the volume. Thus, it would have been obvious to one of ordinary skill in the art at the time of the invention to maintain a constant volume in the vessel of Suzuki (in the process taught by the combination of Suzuki and Lenk) via the addition of the emulsion at the same rate the filtrate is removed, wherein optimization of the rates is within the skill of one in the art.

14. In reference to claims 13 and 14, Lenk discloses that the filter size of the cross flow filter is chosen depending on the size of the particles to be removed (col. 7, lines 29-30), Lenk further shows that the size of the particles filtered depends on the size of the particles input into the filter (col. 8, lines 35-44). Thus the filter size is recognized as a result effective variable. It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize a filter with a pore size in the range of 0.01 to 10 μm (in the process taught by the combination of Suzuki and Lenk), since it has been held that discovering an optimum value as a result effective variable involves only routine skill in the art.

15. In reference to claim 21, the combination of Suzuki and Lenk fail to disclose that the medicament is recovered from the aqueous solution after collection of the microcapsules. It would have been obvious to one of ordinary skill in the art at the time of the invention to extract any medicament contained in the aqueous phase (in the process taught by the combination of Suzuki and Lenk) in order to salvage expensive drugs.

Response to Arguments

16. Applicant's arguments filed 5/27/2008 have been fully considered but they are not persuasive.

17. Applicant has essentially argued that there is no suggestion to combine the references as discussed in the rejection above. Specifically, applicant has argued lack of motivation for the inclusion of the gas separation membrane inside the vessel and accordingly lack of purpose of the cross-flow filter. In response, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

18. Applicant has argued that the cross-flow filter serves no purpose, however, the Lenk reference provides motivation for the inclusion of the cross-flow filer (specifically, as noted in the rejection, sizing of the microcapsules, prevent build-up, remove unentrapped medicament). Applicant has argued that the location of the gas separation membrane inside the vessel serves no purpose, however, the Suzuki reference provides motivation for the inclusion of the gas separation membrane inside the tank (specifically, as noted in the rejection, minimization of clogging). Accordingly, the cross-flow filtration and the gas separation membrane are each recognized as suitable for the same purpose, minimization of clogging/build-up of the emulsion, wherein it is well established that the combination of two methods in order to form a third method useful for the same purpose is *prima facie* obvious. *In re Linder* 457 F, 2d 506,509, 173 USPQ 356, 359 (CCPA 1972).

19. Applicant has argued that the combination of the two methods fails to form a third method that is useful for the same purpose. Specifically, applicants have argued that the combination does not, in fact, form a third method, but one at best no different than before. Firstly, applicant has failed to provide evidence that the combination is inoperable; rather applicant has merely argued inoperability. Secondly, applicant has agreed that the resulting combination third method is no different than before, accordingly, applicant has agreed that the combination of the two methods results in the formation of a third method useful for the same purpose.

20. Hence it is clear that both the cross-flow filtration and inclusion of the gas separation membrane inside the tank function for the same purpose; however, in any instance, each also provides additional advantages to improve the process (as discussed above). Thus, the combination of the two methods results in a third improved method.

21. Applicant has argued that the Suzuki reference failed to disclose that the formed emulsion is transferred to the microsphere storage tank. In response, attention is directed to [0139] of Suzuki which discloses that the emulsion is filled into the vessel, thus the emulsion is transferred into the storage tank (vessel). In reference to applicant's argument regarding the lack of disclosure/teaching of the recycling the filtrate, as noted in the rejection above the saved medicament can readily be utilized in the formation of other microcapsules. Wherein, as set forth in the rejection above, it is necessary that the medicament be present in the emulsion formation step in order for it to be entrapped.

22. In response to applicant's argument that the prior art combination fails to address applicant's alleged advantages, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when

the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAIRA HAIDER whose telephone number is (571)272-3553. The examiner can normally be reached on Monday-Friday from 10am-6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Randy P. Gulakowski can be reached on (571) 272-1302. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Randy Gulakowski/
Supervisory Patent Examiner, Art Unit 1796

Saira Haider
Examiner
Art Unit 1796